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MOUSE FETAL LIVER: A SOURCE OF IMMUNOLOGICALLY REACTIVE CELLS

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ADMINISTRATIVE INFORMATION

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ABSTRACT

Male and female AHeJ mice were mated and the resulting pregnancies were surgically interrupted at various stages of gestation. The embryos were dissected and identical organs (liver, thymus, gut, placenta, and umbilicus) from each separate pregnancy were pooled and injected i. p. into sublethally irradiated (500 rad) F_1 hybrids (either BALB/c x A)F_1 or (C57L x A)F_1). Death of the F_1 hybrids within 60 days was the criterion for the presence of immunologically competent cells in the inoculum. At the end of this period the survivors were sacrificed, their spleens and lymph nodes homogenized, and injected i. p. into sublethally irradiated F_1 hybrids of the other type. Again death within 60 days was the criterion for the presence of immunologically competent cells in the inoculum.

One death occurred among the primary hosts (placenta 1/8). Immunologically competent cells (AHeJ) were detected in secondary recipients of 2nd trimester fetal liver (3/3), 2nd trimester thymus (3/3), and 3rd trimester fetal liver (11/12). No immunologically competent cells (AHeJ) were found in secondary recipients of 3rd trimester and newborn thymus (1/14). Deaths occurred among secondary hosts of fetal gut (3/5), umbilicus (1/3), and placenta (2/9). There were two deaths (2/29) among the secondary control mice. It is concluded that 2nd and

3rd trimester mouse fetal liver, 2nd trimester fetal thymus, and perhaps other fetal tissues contain potential immunologically competent cells. The theoretical significance of these data is discussed.

SUMMARY

The Problem:

Recent observations have focused attention upon the mammalian embryonic and neonatal thymus as a critical organ in the ultimate development of immunological competence. However, other data indicate that mouse fetal liver may be a source of potential immunologically competent cells. The present work adds further evidence for the presence of potential immunologically competent cells in both mouse fetal liver and thymus.

The Findings:

Male and female AHeJ mice were mated and the resulting pregnancies were surgically interrupted at various stages of gestation. The embryos were dissected and identical organs (liver, thymus, gut, placenta, and umbilicus) from each separate pregnancy were pooled and injected i. p. into sublethally irradiated (500 rad)F_1 hybrids (either (BALB/c x A)F_1 or (C57L x A)F_1). Death of the F_1 hybrids within 60 days was the criterion for the presence of immunologically competent cells in the inoculum. At the end of this period the survivors were sacrificed, their spleens and lymph nodes homogenized, and injected i. p. into sublethally irradiated F_1 hybrids of the other type. Again death within

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INTRODUCTION

Recent observations have focused attention upon the embryonic and neonatal thymus as a critical organ in the ultimate development of immunological competence. Kalmutz (1) demonstrated that the opossum embryo was able to react against antigenic stimuli as soon as the thymus had matured, but prior to maturation of other "lymphoid organs". Miller (2), Martinez et al (3) and others (4-7) have shown that mice and rats thymectomized within 24 hours of birth have a markedly reduced life span and a broad impairment of their immunological responsiveness. It has been suggested (2-9) that the fetal thymus and its descendent lymphoepithelial cells, either by the centrifugal distribution of thymocytes which give rise directly to functionally active "collateral" cells, or by some as yet unknown process which promotes proliferation and maturation of locally arising lymphocytic cells, govern the immunological reactivity of the mammalian organism.

However, rodents protected against the lethal effects of X-radiation by the intravenous infusion of isogenic or allogeneic fetal liver cells manifest none of the stigmata of immunological incompetence (10-14). Moreover, Doria et al (15), using 12-18 day mouse embryos, demonstrated that fetal liver "contained potential or actual antibody forming cells" which when transplanted into lethally irradiated hosts, conferred upon them a competent immune system of the donor type. The present communication is intended to add further evidence for the presence of potential

immunologically competent cells in both fetal liver and thymus, and to discuss briefly the possible significance of these and the above cited data.

MATERIALS AND METHODS

The presence of potential immunologically reactive cells in various fetal tissues was determined by the parental-F_1 hybrid, graft-versus-host method of Cole (16), with the following modification. It could be assumed that any immature lymphoid cells which might be present in an inoculum of parental strain fetal tissue would rapidly develop tolerance to their sublethally irradiated F_1 hybrid host, and, as a result, their presence would not be detected. If, however, maturation of these potential immunologically competent cells occurred in the F_1 hybrid host, it should be possible to demonstrate them upon transfer to an F_1 hybrid of another type (one parent in common).

Twelve week old mice, either (C57L x A)F_1 or (BALB/c x A)F_1 (called LAF_1 and CAF_1 respectively), which had received 500 rad whole body X radiation just prior to the i. p. injection of parental strain fetal tissue, were used as primary hosts. Death of these sublethally irradiated F_1 hybrids within 60 days was the criterion for the presence of immunologically competent cells in the inoculum. At the end of this period, each survivor was sacrificed; its spleen and lymph nodes extirpated, lightly homogenized in cold Tyrode's solution, and the cell suspension injected into 1 or 2 sublethally irradiated F_1 hybrids of the other type. Again,

death of the secondary host within 60 days indicated the presence of immunologically reactive parental strain cells in the inoculum. F_1 hybrids (of the same type as the primary host), which had received 500 rad whole body X radiation but no injection of fetal tissue, served as primary radiation controls. Sublethally irradiated F_1 hybrids (of the same type as the secondary host), which received an i. p. injection of spleen and lymph nodes from the primary control animals, were the controls for the secondary hosts. The irradiated mice were housed 4-10 per cage. The diet was Purina Lab Chow, and water (containing 1% Neomycin) was given ad libitum.

Male and female AHeJ mice were mated and the resultant pregnancies were surgically extirpated at various stages of gestation. The embryos were separated from the other products of conception without contamination by maternal blood or tissue, and the various organs under study were dissected free in the cold. Identical organs from a single pregnancy were pooled in cold Tyrode's solution and the cells were dissociated by gentle aspiration through a 23 gauge needle. Where placental tissue was used, the organs were grossly dissected free of maternal decidua, finely minced in cold Tyrode's solution, and the cells were dissociated, by gentle aspiration through a 20 gauge needle. It is doubtful that the placental tissue was entirely free of maternal contamination. The cell suspensions were then injected intraperitoneally into 1 or 2 irradiated F_1 hybrids. Each pregnancy was comprised of from three to nine embryos

of from 11 days gestation to the newly born. The fetal organs used were thymus, liver, gut, umbilicus and placenta. Primary recipients of fetal thymus received from 1 - 10 x 10^6 nucleated cells per animal while recipients of fetal liver received from 25 - 150 x 10^6 nucleated cells. No attempt was made to quantitate the number of gut, umbilicus or placenta cells given.

RESULTS

As can be seen in Table I, one death occurred among the primary hosts (placenta 1/8), indicating: (1) the absence of mature immunologically competent cells in the fetal tissue injected, (2) inadequate numbers of these cells were given, or (3) the potential lymphoid cells in the inoculum were incapable of reactivity in this system. However, deaths did occur among the secondary recipients of fetal liver and thymus from 11 or 12 day gestations (3/3 and 3/3), and among secondary hosts of third trimester fetal liver (11/12). There was one death among the secondary recipients of third trimester and new born thymus (1/14). The deaths occurring among secondary recipients of fetal gut (3/5), umbilicus (1/3) and placenta (2/9) may be explained by contamination with fetal liver, which occurred occasionally during dissection, in the case of gut and umbilicus, and by contamination with maternal tissue in the case of placenta. These latter findings, however, warrant further investigation. There were two deaths (2/29) among the secondary control animals (both occurring in mice housed in the same cage).

DISCUSSION

On the basis of these data and of the observations of Doria et al (15), it is apparent that fetal liver and 2nd trimester fetal thymus contain potential immunologically competent cells, which under the proper conditions are capable of immunological reactivity. These cells were characterized by an apparent initial absence of immunological reactivity in this system and/or an increased ability to become "tolerant" of allogeneic living cells. It should be noted that cells of similar potential were not found in 3rd trimester thymus or in newborn thymus. It is of interest that Delmasso et al (6) in their study of the immunological competence of spleen cells from mice thymectomized during early neonatal life, observed that these cells manifested no reactivity in primary hosts. The present data suggest that such cells might well have exhibited immunological reactivity, had they been transferred to suitable secondary hosts.

That the thymus is not the only source of cells possessing potential immunological competence in the mouse fetus now seems clear. Mouse fetal liver and, perhaps, other fetal tissues (i.e., gut, spleen, lymph nodes) may contain cells which, under the proper circumstances, and when exposed to appropriate stimuli, are capable of immunological reactivity. The mammalian "immune system" may, therefore, be composed of distinct "lines" of cells, phylogenetically derived at different times, which manifest diversity in degree, mode and specificity of their reactivity,

TABLE I

POTENTIAL IMMUNOLOGICALLY COMPETENT CELLS
IN THE LIVER AND THYMUS OF A/HeJ MOUSE EMBRYOS

TRIMESTER OF PREGNANCY	FETAL CELLS INJECTED (A/HeJ)	60-DAY MORTALITY (NO/TOTAL) Primary Host (LAF_1 or CAF_1)	60-DAY MORTALITY (NO/TOTAL) Secondary Host (LAF_1 or CAF_1)	MEAN SURVIVAL TIME (days)
Second*	Thymus	0/2	3/3	15
	Liver	0/2	3/3	26
	Placenta	0/1	1/1	47
	Gut	0/1	0/1	
	None	0/6	0/6	
Third**	Thymus	0/8	1/12	34
	Liver	0/8	11/12	19
	Placenta	1/8	2/9	16
	Gut	0/5	3/5	16
	Umbilicus	0/3	1/3	10
	None	0/32	2/19	10
Newborn$^{\Delta}$	Thymus	0/1	0/2	
	None	0/6	0/4	

*Pooled data from two separate pregnancies (11 and 12 day gestation)

**Pooled data from seven separate pregnancies (18 to 20 day gestation)

$^{\Delta}$One litter of seven

but which in the adult animal occur as an apparently homogeneous cell population. It is proposed that during the 3rd trimester of pregnancy in mice, the lympho-epithelial cells of the thymus differentiate from other potential immunologically competent cells, and that at about the time of birth they migrate to the ultimate sites of immunological reactivity. Here, the thymocytes and their direct descendants, in the adult as well as in the neonate, are not themselves primarily immunologically reactive in the classic sense; however, in some way, as yet unknown they are capable of modifying or augmenting certain lines of lymphoid cells, i.e., by "hormonal" means, or by information transfer, thereby determining the extent, and increasing the specificity of their immunological reactivity.

Thus, one may regard the mammalian thymus as a recent immunological acquisition whose functions include discrimination of fine antigenic differences and the governance of reactivity of certain lines of less sophisticated lymphoid cells.

REFERENCES

1. Kalmutz, S. W., Nature 193, 851 (1962).
2. Miller, J. F. A. P., Lancet II, 748 (1961).
3. Martinez, C., Kersey, J., Papermaster, B. W., and Good, R. A. Proc. Soc. Exp. Biol., N. Y. 109, 193 (1962).
4. Arnason, B. G., Jaukovic, B. D., and Waksman, B. H., Nature 194, 99, (1962).
5. Parrot, D. M. V., Transpl. Bull., 29, 102 (1962).
6. Dalmasso, A. P., Martinez, C., Good, R. A., Proc. Soc. Exp. Biol. and Med. 110, 205 (1962).
7. Papermaster, B. W., Delmasso, A. P., Martinez, C., Good, R. A., Proc. Soc. Exp. Biol. and Med. (1962).
8. Burnet, F. M., Proc. Royal Soc. Med. 55, 619 (1962).
9. Miller, J. F. A. P., Nature 195, 1318 (1962).
10. Congdon, C. C., Urso, I. S., Am. J. Path. 33, 749 (1957).
11. Urso, I. S., Rad. Res. 9, 197 (1958).
12. Barnes, D. W. H., Ilbery, P. L. T., and Loutit, J. F., Nature 181, 488 (1958).
13. Uphoff, D. E., J. Nat. Cancer Inst. 20, 625 (1958).
14. Tschetter, P. N., Githens, J. H., Moscovici, M. G., Blood 18, 182 (1961).
15. Doria, G., Goodman, J. W., Gengozian, N., and Congdon, C. C., J. Immun. 88, 20 (1962).
16. Cole, L. J., and Ellis, M. E., Science 128, 32 (1958).

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4. Mammals.
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II. Cole, L.J.
III. Title.
IV. MR005.08-5200.

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Male and female AHeJ mice were mated and the resulting pregnancies were surgically interrupted at various stages of gestation. The embryos were dissected and identical organs (liver, thymus, gut, placenta, and umbilicus) from each separate pregnancy were pooled and injected i.p. into sublethally irradiated (500 rad) F_1 hybrids (either ((BALB/c x A))F_1 or ((C57L x A))F_1). Death of the F_1 hybrids within 60 days was the criterion for the

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One death occurred among the primary hosts (placenta 1/8). Immunologically competent cells (AHeJ) were detected in secondary recipients of 2nd trimester fetal liver (3/3), 2nd trimester thymus (3/3), and 3rd trimester fetal liver (11/12). No immunologically competent cells (AHeJ) were found in secondary recipients of 3rd trimester and newborn thymus (1/14). Deaths occurred among secondary hosts of fetal gut (3/5), umbilicus (1/3), and placenta (2/9). There were two deaths (2/29) among the secondary control mice. It is concluded that 2nd and 3rd trimester mouse fetal liver, 2nd trimester fetal thymus, and perhaps other fetal tissues contain potential immunologically competent cells. The theoretical significance of these data is discussed.

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